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Claims Listing

1. (Original) A method for detecting an atherosclerotic plaque area of a subject, the method comprising:

administering into the subject a predetermined dose of at least an MRI contrast-enhancing agent that comprises an extended poly(amino acid) conjugated to chelator moieties that form coordination complexes with paramagnetic ions;

obtaining MR images of and acquiring MR signals coming from the subject's blood-vessel wall area surrounding a suspected plaque before and after the step of administering the MRI contrast-enhancing agent into the subject; and

comparing the MR images and MR signals obtained before the step of administering to the MR images and MR signals obtained after the step of administering to identify the blood vessel wall area having an increased MR image contrast and an increased MR signals, which indicate a presence of atherosclerotic plaque.

2. (Original) The method according to claim 1, wherein the poly(amino acid) is selected from the group consisting of homopolymers and copolymers of amino acid residues.

3. (Original) The method according to claim 1, wherein the poly(amino acid) is poly-L-lysine.

4. (Original) The method according to claim 1, wherein the poly(amino acid) is poly(glutamic acid).

5. (Original) The method according to claim 1, wherein the poly(amino acid) comprises a number of amino acid residues in a range from about 100 to about 650.

6. (Original) The method according to claim 1, wherein the poly(amino acid) has a persistence length in a range from about 100 to about 600 angstroms.

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7. (Original) The method according to claim 1, wherein the poly(amino acid) is selected from the group consisting of polyhistidine, polyarginine, polyasparagine, polyglutamine, and copolymers of at least two types of amino acids selected from the group consisting of lysine, histidine, arginine, asparagine, and glutamine.

8. (Original) The method according to claim 1, wherein the poly(amino acid) is a copolymer of glutamic acid and aspartic acid.

9. (Original) The method according to claim 1, wherein the poly(amino acid) is a copolymer of at least a first type of amino acid selected from the group consisting of lysine, histidine, arginine, asparagine, and glutamine; and at least a second type of amino acid selected from the group consisting of glutamic acid and aspartic acid.

10. (Original) The method according to claim 1, wherein the chelator moieties are selected from the group consisting of diethylene triamine pentaacetic acid;

1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid; p-isothiocyanatobenzyl-1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid; 1,4,7,10-tetraazacyclododecane-N,N',N''-triacetic acid; 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetrakis(2-propionic acid); 3,6,9-triaza-12-oxa-3,6,9-tricarboxymethylene-10-carboxy-13-phenyl-tridecanoic acid; 1,4,7-triazacyclononane-N,N',N''-triacetic acid; 1,4,8,11-tetraazacyclotetradecane-N,N',N'',N'''-tetraacetic acid; triethylene tetraamine hexaacetic acid; trans-1,2-diaminohexane tetraacetic acid; 1,4,7,10-tetraazacyclododecane-1-(2-hydroxypropyl)4,7,10-triacetic acid; trans-cyclohexane-diamine tetraacetic acid; trans(1,2)-cyclohexane diethylene triamine pentaacetic acid; 1-oxa-4,7,10-triazacyclododecane-N,N',N''-triacetic acid; 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetrakis{3-(4-carboxyl)-butanoic acid}; 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetrakis(acetic acid-methyl amide); 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetrakis(methylene phosphonic acid); and derivatives thereof.

11. (Original) The method according to claim 1, wherein the chelator moieties are diethylene triamine pentaacetic acid.

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12. (Original) The method according to claim 1, wherein at least 90 percent of residues of the poly(amino acid) are conjugated with the chelator moieties.
13. (Original) The method according to claim 1, wherein at least 95 percent of residues of the poly(amino acid) are conjugated with the chelator moieties.
14. (Original) The method according to claim 12, wherein the chelator moieties are diethylene triamine pentaacetic acid.
15. (Original) The method according to claim 1, wherein the paramagnetic ions are selected from the group consisting of ions of transition metal elements, rare earth metal elements, and actinide elements.
16. (Original) The method according to claim 1, wherein the paramagnetic ions are selected from the group consisting of  $Gd^{3+}$ ,  $Dy^{3+}$ , and a mixture thereof.
17. (Original) The method according to claim 1, wherein said at least an MRI contrast-enhancing agent is administered into the subject at a dose in a range from about 0.01 to about 0.5 mole Gd/kg of body weight of the subject.
18. (Original) The method according to claim 1, wherein the MR images and the MR signals obtained after the step of administering are obtained within 48 hours after said administering.
19. (Original) A method for detecting an atherosclerotic plaque area of a subject, the method comprising:

administering into the subject a predetermined dose of at least an MRI contrast-enhancing agent that comprises an extended poly(amino acid) conjugated to chelator moieties that form coordination complexes with paramagnetic ions, wherein a degree of conjugation is at least 90 percent;

obtaining MR images of and acquiring MR signals coming from the subject's blood-vessel wall area surrounding a suspected plaque before and after the step of administering the MRI contrast-enhancing agent into the subject; and

comparing the MR images and MR signals obtained before the step of administering to the MR images and MR signals obtained after the step of

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administering to identify the blood vessel wall area having an increased MR image contrast and an increased MR signals, which indicate a presence of atherosclerotic plaque;

wherein the poly(amino acid) is selected from the group consisting of poly-L-lysine, polyhistidine, polyarginine, polyasparagine, polyglutamine, poly(glutamic acid), poly(aspartic acid), and copolymers of at least two types of amino acids selected from the group consisting of lysine, histidine, arginine, asparagine, glutamine, glutamic acid, and aspartic acid; the poly(amino acid) has a number of amino acid residues in a range from about 100 to about 650; the chelator moieties are selected from the group consisting of diethylene triamine pentaacetic acid; 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid; p-isothiocyanatobenzyl-1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid; 1,4,7,10-tetraazacyclododecane-N,N',N''-triacetic acid; 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetrakis(2-propionic acid); 3,6,9-triaza-12-oxa-3,6,9-tricarboxymethylene-10-carboxy-13-phenyl-tridecanoic acid; 1,4,7-triazacyclononane-N,N',N''-triacetic acid; 1,4,8,11-tetraazacyclotetradecane-N,N',N'',N'''-tetraacetic acid; triethylene tetraamine hexaacetic acid; trans-1,2-diaminohexane tetraacetic acid; 1,4,7,10-tetraazacyclododecane-1-(2-hydroxypropyl)4,7,10-triacetic acid; trans-cyclohexane-diamine tetraacetic acid; trans(1,2)-cyclohexane diethylene triamine pentaacetic acid; 1-oxa-4,7,10-triazacyclododecane-N,N',N''-triacetic acid; 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetrakis(3-(4-carboxyl)-butanoic acid); 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetrakis(acetic acid-methyl amide); 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetrakis(methylene phosphonic acid); and derivatives thereof; the MRI contrast-enhancing agent is administered into the subject at a dose in a range from about 0.01 to about 0.5 mole Gd/kg of body weight of the subject.

Claims 20-57 (Withdrawn)